

## REMARKS

In the Office Action, claims 1-2 and 4-22 are rejected under 35 U.S.C. § 112, first paragraph; claim 2 is rejected under 35 U.S.C. § 112, second paragraph; claims 1, 2 and 4-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting; and claims 1, 2 and 4-22 are rejected under 35 U.S.C. § 102 or § 103. Claim 2 has been amended. Applicants believe that the rejections have been overcome or are improper in view of the amendments and for the reasons set forth below.

In the Office Action, claims 1, 2 and 4-22 are rejected under 35 U.S.C. § 112, first paragraph. The Patent Office asserts that the microorganism recited in the claims must be obtainable by a repeatable method set forth in the Specification or otherwise be readily available to the public. However, this requirement may be satisfied by a deposit of a microorganism. In this regard, Applicants respectfully submit that a deposit of the microorganism, namely, *Lactobacillus paracasei* CNCM I-2116 (NCC 2461) has been made pursuant to PCT Rule 13 *bis* during the examination of the related International Application No. PCT/EP00/01798. A copy of a document relating to the deposit as discussed above was provided as Exhibit A in Applicants' previously submitted Amendment filed on December 30, 2003. Applicants further submit that the specific strain (e.g. CNCM I-2116) will be irrevocably and without restriction or condition released to the public upon the issuance of a patent. Therefore, Applicants believe that the requirements pursuant to the first paragraph of 35 U.S.C. § 112 have been satisfied.

Accordingly, Applicants respectfully request that the rejection of claims 1, 2 and 4-22 under 35 U.S.C. § 112, first paragraph be withdrawn.

In the Office Action, claim 2 is rejected under 35 U.S.C. § 112, second paragraph. In response, claim 2 has been amended to address the issues raised with respect to this rejection. Applicants believe that the changes to claim 2 were made for clarification purposes and further assert that the changes were further made without intent to narrow or disclaim any claimed subject matter in view of same. Therefore, Applicants believe that claim 2 satisfies the requirements pursuant to 35 U.S.C. § 112, second paragraph. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In the Office Action, claims 1, 2 and 4-22 have been rejected under 35 U.S.C. § 102 or § 103 in view of EP 0861905. Applicants believe that this rejection should be withdrawn as set forth below.

Of the pending claims at issue, claims 1, 7, 9, 11, 12, 20 and 21 are the sole independent claims. Independent claim 1 recites a biologically pure culture of lactic acid bacterium strain belonging to a genus *Lactobacillus* that has the ability to prevent colonization of an intestine with pathogenic bacteria causing diarrhoea and of preventing infection of intestinal epithelial cells by rotaviruses wherein the lactic acid bacterium strain is capable of growing in presence of up to 0.4% bile salts. Claim 7 recites a method for preparing an ingestible support that uses the biologically pure culture of lactic acid bacterium strain. Claim 9 recites a method for preparing an ingestible support material that uses a supernatant of a biologically pure culture of the lactic acid bacterium strain. Claim 11 recites a method for treatment of a disorder associated with diarrhoea that includes administering to a patient having a disorder the biologically pure culture of lactic acid bacterium strain. Claim 12 recites a pharmaceutical composition that contains a biologically pure culture of lactic acid bacterium strain. Claim 20 recites a method for preventing a disorder associated with diarrhoea that includes administering the biologically pure culture of lactic acid bacterium strain. Claim 21 recites a food that includes a biologically pure culture of lactic acid bacterium strain.

The present invention relates to *Lactobacilli* strains that have the ability to prevent colonization of the intestine with both pathogenic bacteria and also against infection of intestinal epithelial cells by rotaviruses. The microorganisms of the present invention have been shown to exhibit a number of desirable properties. They are gram positive, catalase negative,  $\text{NH}_3$  form arginine negative and carbon dioxide production negative. The microorganisms can produce L(+) lactic acid and are capable of growth in the presence of bile salts in a concentration of up to about 0.4% and may effectively prevent infection of epithelial cells by rotaviruses. See, Specification, p. 3, lines 21-25. Further, the probiotic strains of the present invention can essentially survive the passage through the gut, thus arriving in the intestine in an essentially live form so that the strains are readily capable of successfully colonizing the mucosa. Moreover, the claimed strains interact directly with the rotavirus receptors and synthesize metabolites and active compounds that are disadvantageous for the rotaviruses and pathogenic bacteria. See,

Specification, p. 15, Example 5; and p. 16, Example 6. Therefore, the claimed strains provide inhibitory activity against colonization of the intestine with pathogenic bacteria causing diarrhea and infestation of intestinal cells with rotaviruses.

In contrast, Applicants believe that the cited art is distinguishable from the claimed invention. The primary focus of EP0861905 relates to a process which allows selection of Lactobacilli strains that are allegedly viable and resistant to technological treatments, such as freeze-drying or mixing with excipients. The strains are purportedly useful for the therapeutic and prophylactic treatment of disorders of the gastrointestinal system in humans. See, EP0861905, p. 2, line 38 and lines 46-48. For example, the Lactobacilli strains in EP0861905 are purportedly useful in the treatment of various disorders of the gastrointestinal tract, such as peristaltic disorders, gastroenteritis, heartburn, flatulence and diarrhea, particularly diarrhea following the use of antibiotics (See, EP0861905, p.6, lines 7-8) or after an anti-tumor radiotherapy (See, EP0861905, p. 5, line 10).

Indeed, EP0861905 provides that Lactobacilli merely assist in reconstituting the microflora of the intestine or whether they are also providing an activity against some particular agents. In this regard, the clear focus of EP0861905 provides that the strains as disclosed therein are opposing "pathogens", presumably through a lowering of the pH of the intestinal environment. See, EP0861905, p. 4, lines 33-35. As the term "pathogen" is not specifically defined therein, this term can therefore relate to parasites (like worms), fungi, bacteria, viruses or even to particles like prions or of inorganic nature. Thus, the cited art fails to recognize any specific significance to viruses, particularly rotaviruses, let alone the protection property against infection of intestinal epithelial cells by rotaviruses as claimed.

As previously discussed, the cited art provides that Lactobacilli oppose against pathogens through a lowering of the pH of the intestinal environment. See, EP0861905, p. 4, lines 31-35. Yet, it is not clear how the lowering of the pH effects any of the "pathogens" that may be contemplated as embraced by this term as discussed above. Indeed, rotaviruses exhibit a relatively high stability and will presumably not be effected by a relatively small lowering of the pH of the extracellular and intestinal environment caused by organic acids. Thus, a person skilled in the art would conclude that the strains as provided therein (which act by lowering the

pH) are not capable of a prevention of an infection of the human intestine derived from rotaviruses in contrast to the claimed invention.

Further, nowhere does the cited art mention pathogenic bacteria, let alone pathogenic bacteria causing diarrhea and colonizing the intestine. Clearly, the cited art further fails to disclose or suggest that micro-organisms can actively participate in the treatment of diarrhea derived from rotaviruses and simultaneously can protect against pathogenic bacteria causing diarrhea, are present in nature at all, and can be isolated in contrast to the claimed invention. Thus, the cited art fails to recognize such a micro-organism that has the above-mentioned protective properties, that can arrive in the intestine in an essentially live form, that can adhere to the mucosa of the intestine and colonize it and, once implanted in the mucosa (or even before), exert its beneficial effects, such as by interacting with cellular rotavirus receptors and secreting active metabolites into the environment in contrast to the claimed invention. Moreover, the emphasis of the cited art relates to a mixture of strains as disclosed therein (See, EP0861905, p. 5, lines 36-43) and thus effectively teaches against one strain that is effective for treatment purposes as claimed.

Based on at least these differences, Applicants believe one skilled in the art would conclude that the claimed invention is distinguishable from the cited art. Therefore, Applicants respectfully submit that the cited art fails to anticipate or render obvious the claimed invention.

Accordingly, Applicants respectfully request that the anticipation and obviousness rejections in view of EP0861905 be withdrawn.

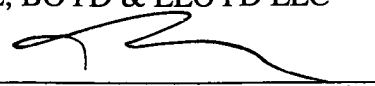
Claims 1, 2 and 4-22 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting. More specifically, claims 1, 2 and 4-22 are provisionally rejected as allegedly being unpatentable over claims 1, 2 and 4-22 of copending application No. 09/936,489 and copending application No. 09/936,453. As the obviousness-type double patenting rejections are provisional, Applicants assert that they plan to submit a terminal disclaimer, if necessary, to overcome the provisional rejections once either one or both of the copending applications have issued. Therefore, Applicants believe that they have been responsive to the provisional rejections at this stage in the prosecution.

For the foregoing reasons, Applicants respectfully submit that the present application is in condition for allowance and earnestly solicit reconsideration for the same.

Respectfully submitted,

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